REMARKS

Claims 1 to 9 and 11 to 14 are pending and under examination in this application. Claim 1 has been amended. Support for the amendments to claim 1 can be found at page 5, line 10, to page 8, line 16.

The Examiner rejected claim 1 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner contends that the step of "contacting the sample with an antibody" is indefinite because it is not clear whether/how said antibody functions in the overall method, or whether said antibody is specific for 25-hydroxy-vitamin D or vitamin D binding protein. In addition, the Examiner states that in step (c), the recitation of "an antibody" is indefinite because it is not clear whether "an antibody" corresponds to "an antibody" recited in step (b).

Applicants respectfully traverse this rejection of the claims. Although Applicants disagree with the Examiner, the claims have been amended to expedite prosecution of this application. Claim 1 now recites that the method comprises an immunoassay in which the antibody is specific for 25-hydroxy-vitamin D and the concentration of 25-hydroxy-vitamin D is determined by determining the amount of 25-hydroxy-vitamin D that is bound by the antibody specific for 25-hydroxy-vitamin D. In addition, the recitation of "an antibody" near the end of claim 1 has been replaced with "the antibody". Accordingly, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

The Examiner rejected claims 1 to 9 and 11 to 13 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,787,660 B1 (Armbruster et al.) in view of U.S. Patent No. 5,382,530 (Romelli et al.). The Examiner states that

Armbruster describes a method for assaying 25-hydroxy-vitamin D in which the vitamin D binding proteins are not removed from the sample before contacting the sample with an antibody (FIG. 7 and column 9, lines 7 to 15) and that Romelli teaches varying the pH of a sample as a means for dissociating vitamins from their respective binding proteins. The Examiner concludes that it would have been obvious to one of skill in the art to use the method for assaying 25-hydroxy-vitamin D as taught by Armbruster with the step of lowering pH as taught by Romelli.

Applicants respectfully traverse this rejection of the claims. The Examiner cites FIG. 7 and column 9, lines 7 to 15, of Armbruster to support the statement that vitamin D binding proteins are not removed from the sample before contacting the sample with an antibody. This portion of Armbruster does not support this statement. FIG. 7 shows an assay which is free of vitamin D binding protein. Vitamin D binding protein is not shown in FIG. 7 or described in column 9, lines 7 to 15. Compare these portions of the specification with FIG. 6 and column 9, lines 1 to 6, which show and describe vitamin D binding protein. FIG. 6 and column 9, lines 1 to 6, were cited in the December 3, 2004 Office Action to support this rejection. The embodiment of FIG. 7 of Armbruster will be discussed first, and then the embodiment of FIG. 6 will be addressed.

As described in the specification of the application under examination, the vitamin D binding protein must be dissociated from the 25-hydroxy-vitamin D to make it available for analysis using an antibody to Vitamin D. The specification states:

> Due to the relatively high plasma concentration of the Vitamin D binding protein, which has an affinity similar to that of antibodies,

> the 25-OH Vitamin D must be dissociated from the binding protein to make it available for analysis in the sample. Historical methods for accomplishing this rely on denaturing the Vitamin D binding protein with organic solvents (sometimes preceded by the use of ammonium sulfate to precipitate the Vitamin D binding protein). The Vitamin D binding proteins are then removed from the assay to enable antibody binding to Vitamin D.

Page 2, lines 11 to 18.

In the assay shown in FIG. 7 of Armbruster, which uses an antibody to Vitamin D, the vitamin D binding proteins appear to have been removed since they are neither shown in FIG. 7 nor mentioned in column 9, lines 7 to 15. This is consistent with the above quote from the specification of the application under examination.

The assay of FIG. 7 of Armbruster does not mention or show vitamin D binding proteins at all. The vitamin D binding proteins appear to have been removed from the sample before contacting the sample with the antibody to vitamin D. The pending claims require that the vitamin D binding proteins are not removed from the sample before contacting the sample with the antibody specific for 25-hydroxy-vitamin D. Accordingly, Armbruster does not teach or suggest the claimed invention in which the vitamin D binding proteins are not removed from the sample before contacting the sample with the antibody specific for 25-hydroxy-vitamin D.

Romelli does not remedy this defect of Armbruster. First, there is no suggestion in Armbruster or Romelli to combine these references to arrive at a test for vitamin D in which the pH of the sample is lowered to dissociate the vitamin D from the vitamin D binding proteins and in which the vitamin D binding proteins

are not removed from the sample before contacting the sample with the antibody specific for 25-hydroxy-vitamin D.

Second, even if the references are combined, the claimed invention still is not suggested to one of skill in the art. Column 9, lines 7 to 15, of Armbruster describes an assay in which the vitamin D binding proteins have already been removed prior to contacting the sample with the antibody specific for 25-hydroxy-vitamin D. Romelli teaches investigating pH to dissociate a ligand from an analyte. The combination of Armbruster with Romelli does not suggest the claimed invention because Armbruster (FIG. 7) removes the vitamin D binding proteins before contacting the sample with the antibody specific to vitamin D and Romelli does not suggest modifying the vitamin D assay of Armbruster (FIG. 7) to include the presence of vitamin D binding proteins, which is required by the claims.

As discussed in the April 1, 2005 Amendment and Response, the embodiment of FIG. 6 of Armbruster shows a competitive protein binding test in which 25-OH-vitamin-D_3-biotin and 25-OH-vitamin D (from a standard or sample) compete in liquid phase for the binding site of the vitamin D binding protein. See column 9, lines 1 to 6. Armbruster describes an immunoassay without any lowering of pH. Accordingly, Armbruster does not teach or suggest the claimed invention in which the pH of the sample is lowered to dissociate the 25-hydroxy-vitamin D from vitamin D binding proteins.

Romelli does not remedy this defect of Armbruster. First, there is no suggestion in Armbruster or Romelli to combine these references to arrive at a test for vitamin D in which the pH of the sample is lowered to dissociate the vitamin D from the vitamin D binding proteins. Second, even if the references are combined,

the claimed invention still is not suggested to one of skill in the art. The competitive protein binding test shown in FIG. 6 and described at column 9, lines 1 to 6, of Armbruster in which the vitamin D binding proteins are not removed from the sample will not function if the pH of the sample is lowered to dissociate the vitamin D from the vitamin D binding proteins.

The competitive protein binding test of Armbruster functions because the labeled vitamin D and the unlabeled vitamin D from a sample compete to bind with the vitamin D binding proteins. If the vitamin D does not bind with the vitamin D binding proteins, nothing meaningful is measured. The combination of Armbruster (FIG. 6) and Romelli does not suggest to one of skill in the art the claimed invention because the combination of Armbruster and Romelli does not result in a functioning assay.

The combination of Armbruster (embodied in FIG. 6 or FIG. 7) and Romelli does not teach or suggest an assay in which the vitamin D binding proteins are not removed from the sample before contacting the sample with the antibody specific for 25-hydroxy-vitamin D. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

The Examiner rejected claim 14 under 35 U.S.C. § 103(a) as being unpatentable over Armbruster in view of Romelli, as applied to claims 1 and 13, and further in view of Schroeder et al., 57 Methods Enzymol. 424-445 (1978).

Applicants respectfully traverse this rejection of the claims. Claim 14 depends from claim 1. As noted above in the discussion of the rejection of claims 1 to 9 and 11 to 13 as unpatentable over Armbruster and Romelli, neither of these documents or their combination teaches or suggests the invention of claim 1. Schroeder does not remedy this deficiency of Armbruster and Romelli.

Accordingly, Applicants respectfully request that the Examiner withdraw this rejection of the claims.

In view of the above amendments and remarks, Applicants respectfully request that the Examiner withdraw the rejections of the claims.

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Respectfully submitted,

Date: September 7, 2005

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